General

Guideline Title

Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 25 p. (Clinical guideline; no. 143).

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Centre for Clinical Practice at the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Individualised Assessment at Presentation

Treat an acute painful sickle cell episode as an acute medical emergency. Follow locally agreed protocols for managing acute painful sickle cell episodes and/or acute medical emergencies that are consistent with this guideline.

Throughout an acute painful sickle cell episode, regard the patient (and/or their carer) as an expert in their condition, listen to their views and discuss with them:

- The planned treatment regimen for the episode
- Treatment received during previous episodes
- Any concerns they may have about the current episode
- Any psychological and/or social support they may need

Assess pain and use an age-appropriate pain scoring tool for all patients presenting at hospital with an acute painful sickle cell episode.

Offer analgesia within 30 minutes of presentation to all patients presenting at hospital with an acute painful sickle cell episode (see also recommendations below).

Clinically assess all patients presenting at hospital with an acute painful sickle cell episode, including monitoring of:

- Blood pressure
- Oxygen saturation on air (if oxygen saturation is 95% or below, offer oxygen therapy)
- Pulse rate
- Respiratory rate
- Temperature

Assess all patients with sickle cell disease who present with acute pain to determine whether their pain is being caused by an acute painful sickle cell episode or whether an alternative diagnosis is possible, particularly if pain is reported as atypical by the patient.

Primary Analgesia

When offering analgesia for an acute painful sickle cell episode:

- Ask about and take into account any analgesia taken by the patient for the current episode before presentation
- Ensure that the drug, dose and administration route are suitable for the severity of the pain and the age of the patient
- Refer to the patient's individual care plan if available

Offer a bolus dose of a strong opioid by a suitable administration route, in accordance with locally agreed protocols for managing acute painful sickle cell episodes, to:

- All patients presenting with severe pain
- All patients presenting with moderate pain who have already had some analgesia before presentation

Consider a weak opioid as an alternative to a strong opioid for patients presenting with moderate pain who have not yet had any analgesia.

Offer all patients regular paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) by a suitable administration route, in addition to an opioid, unless contraindicated. (The use of NSAIDs should be avoided during pregnancy, unless the potential benefits outweigh the risks. NSAIDs should be avoided for treating an acute painful sickle cell episode in women in the third trimester. See the "British National Formulary" for details of contraindications.)

Do not offer pethidine for treating pain in an acute painful sickle cell episode.

Reassessment and Ongoing Management

Assess the effectiveness of pain relief:

- Every 30 minutes until satisfactory pain relief has been achieved, and at least every 4 hours thereafter
- Using an age-appropriate pain scoring tool
- By asking questions, such as:
    - How well did that last painkiller work?
    - Do you feel that you need more pain relief?

If the patient has severe pain on reassessment, offer a second bolus dose of a strong opioid (or a first bolus dose if they have not yet received a

strong opioid).

Consider patient-controlled analgesia if repeated bolus doses of a strong opioid are needed within 2 hours. Ensure that patient-controlled analgesia is used in accordance with locally agreed protocols for managing acute painful sickle cell episodes and/or acute medical emergencies.

Offer all patients who are taking an opioid:

- Laxatives on a regular basis
- Anti-emetics as needed
- Antipruritics as needed

Monitor patients taking strong opioids for adverse events, and perform a clinical assessment (including sedation score):

- Every 1 hour for the first 6 hours
- At least every 4 hours thereafter

If the patient does not respond to standard treatment for an acute painful sickle cell episode, reassess them for the possibility of an alternative diagnosis.

As the acute painful sickle cell episode resolves, follow locally agreed protocols for managing acute painful sickle cell episodes to step down pharmacological treatment, in consultation with the patient.

Possible Acute Complications

Be aware of the possibility of acute chest syndrome in patients with an acute painful sickle cell episode if any of the following are present at any time from presentation to discharge:

- Abnormal respiratory signs and/or symptoms
- Chest pain
- Fever
- Signs and symptoms of hypoxia:
    - Oxygen saturation of 95% or below
    - An escalating oxygen requirement

Be aware of other possible complications seen with an acute painful sickle cell episode, at any time from presentation to discharge, including:

- Acute stroke
- Aplastic crisis
- Infections
- Osteomyelitis
- Splenic sequestration

Management of Underlying Pathology

Do not use corticosteroids in the management of an uncomplicated acute painful sickle cell episode.

Non-pharmacological Interventions

Encourage the patient to use their own coping mechanisms (for example, relaxation techniques) for dealing with acute pain.

Settings and Training

All healthcare professionals who care for patients with an acute painful sickle cell episode should receive regular training, with topics including:

- Pain monitoring and relief
- The ability to identify potential acute complications
- Attitudes towards and preconceptions about patients presenting with an acute painful sickle cell episode

Where available, use daycare settings in which staff have specialist knowledge and training for the initial assessment and treatment of patients presenting with an acute painful sickle cell episode.

All healthcare professionals in emergency departments who care for patients with an acute painful sickle cell episode should have access to locally

agreed protocols and specialist support from designated centres.

Patients with an acute painful sickle cell episode should be cared for in an age-appropriate setting.

For pregnant women with an acute painful sickle cell episode, seek advice from the obstetrics team and refer when indicated.

Discharge Information

Before discharge, provide the patient (and/or their carer) with information on how to continue to manage the current episode, including:

- How to obtain specialist support
- How to obtain additional medication
- How to manage any potential side effects of the treatment they have received in hospital

Clinical Algorithm(s)

A NICE Pathway on sickle cell acute painful episode is provided at the National Institute for Health and Clinical Excellence (NICE) Web site .

Scope

Disease/Condition(s)

- Sickle cell disease (acute painful episode)
- Complications of acute painful sickle cell episode

Guideline Category

Management

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Hematology

Internal Medicine

Pediatrics

Pharmacology

Intended Users

Advanced Practice Nurses

Emergency Medical Technicians/Paramedics

Health Care Providers

Hospitals

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To provide best practice advice on the care of adults, young people and children presenting at hospital with an acute painful sickle cell episode

Target Population

All patients with an acute painful sickle cell episode including children, young people, and pregnant women

Interventions and Practices Considered

1. Assessment of pain and use of an age-appropriate pain scoring tool
2. Offering analgesia within 30 minutes of presentation
    - Strong opioid
    - Weak opioid
    - Non-steroidal anti-inflammatory drug (NSAIDs) and paracetamol
3. Clinical assessment including monitoring of blood pressure, oxygen saturation on air, pulse rate, respiratory rate, temperature
4. Reassessment of pain and ongoing management
5. Use of laxatives on a regular basis and anti-emetics and antipruritics as needed in patients taking opioids
6. Monitoring for adverse effects of opioids, including sedation
7. Monitoring for acute chest syndrome and other acute complications at any time from presentation to discharge
8. Managing of underlying pathology (corticosteroids not recommended)
9. Use of non-pharmacological interventions such as relaxation techniques for pain management
10. Training of healthcare personnel who care for patients with an acute painful sickle cell episode
11. Caring for patients in an age-appropriate setting
12. Seeking advice from obstetrics for pregnant women
13. Providing patients and/or carers with appropriate discharge information

Major Outcomes Considered

- Survival
- Intensity and duration of pain using validated and age-appropriate pain rating scales
- Amount of analgesia used
- Development of acute complications
- Treatment-associated adverse events
- Length of hospital stay
- Patient and carer satisfaction or experience of pain management
- Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Centre for Clinical Practice at the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Clinical Effectiveness

Literature Search

For all review questions, papers were identified from one database using a broad search strategy and included all papers relating to acute pain in sickle cell disease.

See appendix D in the full version of the original guideline for additional information about the literature search (including search strategies used) and a full list of excluded papers.

Review question 1: How should an acute painful sickle cell episode be managed using pharmacological interventions?

This review question focused on the use of pharmacological interventions to manage an acute painful sickle cell episode. This includes the timing, choice and route of administration of drugs, the use of patient-controlled analgesia (PCA), and the timing and frequency of monitoring of pain and physiological measures. Pharmacological interventions include primary analgesic treatments that are used to manage pain, such as non-steroidal anti-inflammatory drugs (NSAIDs), non-opioids, strong opioids (such as morphine, which is used to treat severe pain) and weak opioids (such as codeine, which is used to treat mild to moderate pain). The use of other pharmacological interventions to manage the underlying sickling process was also assessed: these included corticosteroids, low-molecular-weight heparin (LMWH) and oxygen, all of which are provided in addition to analgesia. This review question also assessed the use of different modes of delivery, including PCA, intramuscular injection, and intravenous (including intermittent intravenous injection and continuous infusion) and oral routes of administration.

Only randomised controlled trials (RCTs) that compared a pharmacological intervention with either a placebo or another comparator in patients having an acute painful sickle cell episode were considered for inclusion. From a database of 5534 abstracts, 232 full-text articles were ordered and 20 papers describing 19 primary studies were selected.

Trials were excluded if they:

- Focused on reducing the incidence of acute painful sickle cell episodes
- Used unlicensed drugs
- Used unclear measurements of pain
- Were carried out in settings other than hospital, for example in the community

Review question 2: Which non-pharmacological interventions should be used in the management of an acute painful sickle cell episode?

This review question focused on the use of non-pharmacological interventions such as distraction and relaxation techniques, acupuncture, TENS (transcutaneous electrical nerve stimulation) and heat therapy in the management of an acute painful sickle cell episode. Only RCTs that compared a non-pharmacological intervention with either a placebo or another comparator in patients having an acute painful sickle cell episode were considered for inclusion. From a database of 5534 abstracts, 232 full-text articles were ordered and one paper was selected. Trials were excluded if they:

- Focused on reducing the incidence of acute painful sickle cell episodes
- Used unclear measurements of pain
- Were carried out in settings other than in hospital, for example in the community

Review question 3: What clinical signs and symptoms should be used to identify patients who are likely to have acute complications associated with an acute painful sickle cell episode?

This review question focused on the use of clinical signs and symptoms and laboratory markers to identify acute complications in patients who present to hospital with an acute painful sickle cell episode. This question did not aim to identify all risk factors for the development of acute complications, but was limited to clinical signs and symptoms and laboratory markers that may be present during hospitalisation. Studies assessing

other risk factors such as demographic characteristics were not included. As this question was restricted to specific risk factors, studies assessing these factors using any comparative analyses were included. The formal diagnosis of acute complications was specifically excluded as this was outside the scope of the guideline.

From a database of 5534 abstracts, 140 full-text articles were ordered and 13 papers were selected for this review question.

Studies were excluded if they:

- Focused on risk factors for acute complications in patients in the "steady state" of sickle cell disease
- Focused on the prevention or management of acute complications
- Did not provide comparative analyses (that is, they were narrative reviews, case studies or case series)

No specific studies were identified that focused on the effect of identifying acute complications on subsequent survival rates.

Review question 4:

- a) Where should an acute painful sickle cell episode be managed?
- b) What skills and knowledge are required by healthcare professionals and teams providing care?

This review question focused on identifying the best setting in which to manage an acute painful sickle cell episode and the skills required by healthcare professionals. Any papers focusing on the organisation of care or the skills and/or knowledge of healthcare professionals were considered for inclusion for this review question. From a database of 5534 abstracts, 78 full-text articles were ordered and eight papers were selected.

Trials were excluded if they:

- Focused on the use of a clinical pathway without reference to the organisation of care or the skills and knowledge of healthcare professionals
- Related to the management of an acute painful sickle cell episode in the community.

Review question 5: What information do people need during an acute painful sickle cell episode?

This review question considered the information and support needs of patients and their family members and/or carers during an acute painful sickle cell episode. From a database of 5534 studies, 69 articles were ordered. A further two articles were identified from a systematic review, leaving a total of 71 papers for consideration.

Studies were considered for inclusion if they were related to an acute painful sickle cell episode within the hospital setting and covered education, patient experiences and/or information needs. As the scope of the guideline considered the management of sickle cell episodes in hospital, any paper that focused on management of an acute painful episode at home was excluded. There was no restriction on study design, although only full papers were eligible for inclusion.

Ten full-text articles from nine primary studies met the eligibility criteria and were included in the final review. All of the included studies were qualitative in design (incorporating patient focus groups and/or interviews) or patient questionnaires, or a mix of the two designs.

Health Economics

A search for published health economic analyses addressing the questions of interest yielded a total of 1189 unique citations. However, none of these studies analysed both the costs and health consequences of the alternative modes of managing an acute painful sickle cell episode (for details, please see appendix F in the full version of the original guideline). In the absence of relevant published literature, an original health economic model was constructed.

Number of Source Documents

- Review question 1- 20 papers describing 19 primary studies were selected.
- Review question 2 - one paper was selected.
- Review question 3 - 13 papers were selected.
- Review question 4 - eight papers were selected.
- Review question 5 - ten full-text articles from nine primary studies met the eligibility criteria.
- Cost effectiveness - an economic model was presented.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

The quality of the evidence was based on the quality assessment components (study design, limitations to study quality, consistency, directness and any other considerations) and graded using the following definitions:

- High - Further research is very unlikely to change the confidence in the estimate of the effect.
- Moderate - Further research is likely to have an important impact on the confidence in the estimate of the effect and may change the estimate.
- Low - Further research is very likely to have an important impact on the confidence in the estimate of the effect and is likely to change the estimate.
- Very low - Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Centre for Clinical Practice at National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Clinical Effectiveness

Review Question 1: How should an acute painful sickle cell episode be managed using pharmacological interventions?

The Guideline Development Group (GDG) selected outcomes as 'critical' or 'important' after evidence synthesis. At the GDG meeting, the outcomes and their relative importance were discussed. It was agreed that pain rating, amount of analgesia used, use of additional or rescue doses of analgesia, length of stay in hospital and adverse events were considered 'critical' to decision making, while the duration of the acute painful sickle cell episode and readmission were outcomes that were 'important' to decision making.

There was limited pooling of studies, because a number of different interventions were being assessed and there was heterogeneity across the included studies. Where meta-analysis was possible, a forest plot is also presented (see appendix E in the full version of the original guideline). Where sufficient data were available, mean differences (MDs) were calculated for continuous outcomes and relative risks (RRs) for binary outcomes. Results from other categorical outcomes were summarised from the papers.

Two full Grading of Recommendations: Assessment, Development, and Evaluation (GRADE) tables are presented for this review question: one for primary analgesia and one for treatments managing the underlying pathology of the sickling process (see appendix E in the full version of the original guideline). Summary GRADE tables divided by intervention are presented in the full version of the original guideline.

Review Question 2: Which non-pharmacological interventions should be used in the management of an acute painful sickle cell episode?

Only one paper was included (see Table 23 in the full version of the original guideline), so no meta-analysis was carried out and a single GRADE table (see Table 24) is presented in the full version of the original guideline.

Review Question 3: What clinical signs and symptoms should be used to identify patients who are likely to have acute complications associated with an acute painful sickle cell episode?

Because GRADE has not been developed for use with prognostic studies, a modified approach was used based on the use of GRADE for diagnostic studies. The same criteria (risk of bias, inconsistency, imprecision and indirectness) were used to downgrade the quality of the evidence. In terms of study design, prospective studies were started with a high-quality rating, whereas retrospective studies were started with a low-quality rating and downgraded as appropriate. This is because there is a higher risk of information bias associated with retrospective study designs.

Quality ratings were downgraded further for risk of bias if there was evidence of selection bias. Inconsistency was assessed by examining unexplained differences in estimates of effect. In this case, a range of different estimates of effect were reported, including diagnostic accuracy statistics, statistical measures of association or adjusted odds ratios from multivariate regression analyses. Indirectness was assessed by examining any important differences in population, prognostic factor or outcome of the included evidence compared with those for whom the recommendation is intended. Imprecision was assessed by examining the sample size or the 95% confidence intervals around the estimate of effect. Although GRADE provides rules of thumb when assessing imprecision in intervention questions (that is, where the total sample size is less than 400, the event rate is less than 300 or the 95% confidence intervals cross the thresholds for appreciable benefit or harm or the minimal important difference), these may not be directly applicable to prognostic studies. For this review question the evidence was downgraded for imprecision where 95% confidence intervals (if reported or calculated) were wide. This criterion was met if the interval was not narrow enough to support a recommendation or the final recommendation would change if the effect estimate was equal to the lower 95% boundary. Where no confidence intervals were reported, small sample size was used as a criterion for downgrading. As sample sizes were small for all included studies (less than 400) the evidence was generally downgraded for imprecision even if confidence intervals were relatively narrow.

Six modified GRADE tables are presented in the full version of the original guideline (see Tables 26-31), one for each acute complication examined in the included studies.

For the Review Question 4, (a) "Where should an acute painful sickle cell episode be managed?" (b) "What skills and knowledge are required by healthcare professionals and teams providing care?", several papers did not report any statistical analyses, but results are summarised in the GRADE profile for those that did. Mean differences were not calculated in papers where the standard deviation (SD) was not reported. There was limited pooling because there was heterogeneity across the included studies. Where meta-analysis was possible, a forest plot is also presented (see Appendix E in the full version of the original guideline [see the "Availability of Companion Documents" field). A single GRADE table is presented for this review question (see Table 33 in the full version of the original guideline).

Review Question 5: What information do people need during an acute painful sickle cell episode?

The quality of all included studies was assessed using appropriate methodology checklists. The qualitative designs were assessed by using the relevant NICE methodology quality appraisal checklist. There is currently no checklist available for the assessment of survey or questionnaire designs. Therefore a checklist originally published in the British Medical Journal was modified to aid the quality assessment of these studies (see Appendix E in the full version of the original guideline for a copy of this checklist).

Because GRADE methodology has not yet been adapted for use with qualitative studies, a thematic analysis was undertaken. All of the included studies were initially screened to identify common key themes and issues relating to patient experiences during admission for an acute painful sickle cell episode. The evidence was then further explored to identify common subthemes across all 10 papers. All papers were then re-examined to ensure that all relevant key themes and subthemes were extracted. These key themes and subthemes were then used to identify the information and support needs of patients and their carers during an acute painful sickle cell episode in hospital.

Two studies were considered to provide a thorough reporting of the study design, data collection, validity and reliability of the research findings. The majority of the reviewed papers did, however, have some limitations. The main sources of bias were identified with study validity. Most papers did not adequately report the role of the researcher or consider the impact this could have upon participants' responses. Additionally, several papers did not describe the settings and context in which the research was undertaken in great detail. Any study-specific limitations identified by the quality assessment are included within the summary of included studies table (see Table 35 in the full version of the original guideline). The key themes and subthemes identified across all studies are shown within a key themes matrix, which provides a more detailed overview of the themes and issues identified within each study (see Table 36 in the full version of the original guideline).

Health Economics

In the absence of relevant published literature, an original health economic model was constructed for pharmacological interventions.

Decision Problems

Two questions were addressed, based on the literature that had been identified in the review of clinical effectiveness evidence:

- What is the cost effectiveness of administering morphine via patient-controlled analgesia (PCA), compared with continuous intravenous infusion of morphine (C-IV)?
- What is the cost effectiveness of low-molecular-weight heparin (LMWH) as an adjunct to standard care, when compared with standard care alone?

Both questions were explored using the same model structure and, as far as the underlying simulation of an acute painful sickle cell episode was concerned, the same model parameters.

See section 2.1.4 and Appendix F in the full version of the original guideline for details of the modelling carried out for the guideline.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the Centre for Clinical Practice at National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Forming and Running the Short Clinical Guideline Development Group (GDG)

Each short clinical guideline is developed by a unique GDG consisting of 10–12 members, supported by the Short Clinical Guidelines Team. Each GDG has a Chair, healthcare professional members and a minimum of two patient and carer members. Co-opted expert advisers are recruited, as appropriate. A Clinical Adviser, who has specific content expertise and additional responsibilities, may also be appointed depending on the topic. Recruitment of the GDG Chair and members is carried out in accordance with NICE's policy.

The GDG makes its decisions using the best available evidence presented to it at GDG meetings by the Short Clinical Guidelines Team. The use of formal consensus methods within the GDG will be considered on a case-by-case basis.

Developing Review Questions

A short clinical guideline has a narrow scope and covers only part of a care pathway. It addresses a maximum of three subject areas covering clinical management. This will result in a small number of key clinical issues. These are broken down into a defined number of review questions — usually one or two per clinical management area. The exact number will be dictated by the size of the short clinical guideline remit and the amount of development time available.

Creating Guideline Recommendations

Explicit methods of linking the evidence to recommendations are used for short clinical guidelines if the topic is suitable. This involves using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Research recommendations are formulated for short clinical guidelines. Their number is dependent on the size of the short clinical guideline remit and the amount of development time available.

Writing the Guideline

There are usually three versions of short clinical guidelines:

- The full guideline – all the recommendations, details of how they were developed and summaries of the evidence they are based on.
- The quick reference guide – a summary of the recommendations for healthcare professionals.
- 'Understanding NICE guidance' – a summary for patients and carers.

The full guideline is written by the Short Clinical Guidelines Team, following the principles in chapters 9 and 10 of 'The guidelines manual' (see the "Availability of Companion Documents" field).

See Appendix D of the full guideline for the review questions and review protocols for this guideline.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Two questions were addressed, based on the literature that had been identified in the review of clinical effectiveness evidence:

- What is the cost effectiveness of administering morphine via patient-controlled analgesia (PCA), compared with continuous intravenous infusion of morphine (C-IV)?
- What is the cost effectiveness of low-molecular-weight heparin (LMWH) as an adjunct to standard care, when compared with standard care alone?

An original health economic model was constructed. The model used a Markov structure, capturing costs and effects associated with a series of discrete health states. Figure 1 in the full version of the original guideline presents a simplified representation of the model structure, which was based on the natural history of an acute painful sickle cell episode and inputs from the Guideline Development Group (GDG).

The model was constructed in Microsoft Excel 2010. Costs and benefits were discounted at 3.5% per annum each.

PCA Compared with C-IV

Deterministic and probabilistic analyses strongly suggest that, when compared with morphine delivered by C-IV, morphine delivered by PCA is likely to be the cheaper and most effective (dominant) approach.

However, GDG opinion suggests that C-IV administration of morphine is not very common in UK practice, and that a more realistic comparator for PCA would be the intermittent injection of morphine via an intramuscular or subcutaneous route. However, there are no data on the effectiveness of an intermittent regimen, so this comparator could not be incorporated in the cost–utility model. For this reason, an additional cost-minimisation analysis was performed exploring differences in resource-use between PCA and intermittent approaches.

The analysis did not account for the purchase price of PCA pumps, as prices are variable, and many hospital units already have access to pumps that have been acquired for other indications. However, it was calculated that the expected cost savings would offset an average purchase price of around £2500 (personal communication from manufacturer of one type of PCA pump), if it was assumed that each pump would be used for a minimum of between two and nine acute painful sickle cell episodes (depending on the scenario adopted in the analyses).

LMWH

Deterministic and probabilistic analyses strongly suggest that, if the evidence from a reported Saudi Arabian randomised controlled trial (RCT) can be assumed to generalise to the UK setting, the use of LMWH would both reduce costs and improve outcomes, making it excellent value for money. However, these results should be treated with substantial caution. The provision of healthcare in Saudi Arabia and the characteristics of the trial participants are likely to be very different from those encountered in the UK.

Moreover, in the UK, adult patients who are admitted for an acute painful sickle cell episode routinely receive a low dose of LMWH as prophylaxis against venous thromboembolism. Therefore a placebo-controlled RCT does not provide applicable evidence for the UK decision-making context: prophylactic-dose LMWH would be the relevant comparator against which to assess the clinical and cost effectiveness of therapeutic-dose LMWH in UK practice.

For this reason, the effectiveness of therapeutic-dose LMWH in this analysis may have been substantially overestimated. However, the model shows that, even if relatively modest health gains could be achieved by therapeutic-dose LMWH in comparison with prophylactic-dose LMWH, the routine use of the higher dose could be expected to represent an effective use of National Health Service resource.

Refer to Section 2.1.4 and 2.4.4 in the full version of the original guideline for more information. See also Appendix F for the full health economic report.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline, National Institute for Health and Clinical Excellence [NICE] guideline, and Quick Reference

Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG).
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of an acute painful sickle cell episode in hospital

Potential Harms

Adverse events of medications

Contraindications

Contraindications

The use of non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided during pregnancy, unless the potential benefits outweigh the risks. NSAIDs should be avoided for treating an acute painful sickle cell episode in women in the third trimester. See the 'British National Formulary' for details of contraindications.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- This is an overarching guideline covering the principles of how to manage an acute painful sickle cell episode in hospital. Local protocols should be referred to for specific management plans, including drug choice and dosages. This guideline includes the management of acute painful sickle cell episodes in children and young people and in pregnant women. The guideline recommendations apply to all patients presenting with an acute painful sickle episode unless there are differences in management for these groups, in which case these are clearly

outlined.

- The guideline does not make recommendations on drug dosage; prescribers should refer to the 'British national formulary (BNF)' and 'BNF for children' for this information. The guideline also assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Implementation of the Guideline

Description of Implementation Strategy

National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance (see http://guidance.nice.org.uk/CG143 ; see also "Availability of Companion Documents" field).

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 25 p. (Clinical guideline; no. 143).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Jun

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence

Guideline Committee

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Financial Disclosures/Conflicts of Interest

All Guideline Development Group (GDG) members and external advisers potential and actual conflicts of interest were recorded on declaration forms provided by the National Institute for Health and Clinical Excellence (NICE) (summarised in Appendix A of the full version of the original guideline). None of the interests declared by GDG members constituted a material conflict of interest that would influence recommendations developed by the GDG.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. 179 p. (Clinical guideline; no. 143). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .
- Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital. Appendices to full version. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. (Clinical guideline; no. 143). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site .
- Sickle cell acute painful episode. Electronic audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. (Clinical guideline; no. 143). Electronic copies: Available from the NICE Web site .
- Sickle cell acute painful episode. Clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. 10 p. (Clinical guideline; no. 143). Electronic copies: Available from the NICE Web site .
- Sickle cell acute painful episode. Baseline assessment tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. (Clinical guideline; no. 143). Electronic copies: Available from the NICE Web site .
- Sickle cell acute painful episode. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. 24 p. (Clinical guideline; no. 143). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site .
- Sickle cell acute painful episode. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. 24 p. (Clinical guideline; no. 143). Electronic copies: Available from the NICE Web site .
- Sickle cell acute painful episode overview. Nice pathway. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 June. (Clinical guideline; no. 143). Available from the NICE Web site .
- The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available in Portable Document Format (PDF) from the NICE Archive Web site .

Patient Resources

The following is available:

- Treating acute painful sickle cell episodes in hospital. Understanding NICE guidance. Information for people who use NHS services. 2012 Jun. 11 p. Available in Portable Document Format [PDF] format from the National Institute for Health and Clinical Excellence (NICE) Web site .

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NGC Status

This summary was completed by ECRI Institute on September 4, 2012. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

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